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EXAMINER	
ARCHIE, NINA	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

PTOL-90A (Rev. 04/07)

Office Action Summary	**Application No.** 10/682,130	**Applicant(s)** KLINMAN ET AL.
	Examiner Nina A. Archie	**Art Unit** 1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,10,12,13,16,18,35,43-47,50,54 and 57-60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *46,47,54 and 60* is/are allowed.

6)☒ Claim(s) *1-5,10,12,13,16,18,35,43-45 and 57-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office Action is responsive to Applicant's amendment and response filed on 5/19/2009 has been entered into the record. Claims 1-5, 10, 12-13, 16, 18, 35, 43-47, 50, 54, 57-60 are pending and under examination.

Objections/Rejections Withdrawn

2. In view of the Applicant's amendment and remark following objections/rejections are withdrawn.

a) Objections to claims 22 and 24 because of the following informalities: IL-6, MIP-2, etc. the claims contain acronyms is withdrawn in light of cancellation of claims.

b) Rejections to claims 19-28, 33, 36, 39, 41, 49, 51-53, 55-56 under 35 U.S.C. 102 (b) as being anticipated by West et al WO/1993/023572 Date November 25, 1993 is withdrawn in light of cancellation of claims.

Election/Restrictions

3. Examiner has withdrawn the election of species in the restriction on 7/21/2006. Applicant timely traversed the restriction (election) requirement in the reply filed on 8/23/06.

Allowable subject matter and Interview Summary

Applicant arguments:

4. Applicants state Claims 35, 43-47, 50 and 54 were objected to for depending on a rejected base claim, but were indicated to be allowable if amended to be in independent form or to depend from an allowable claim. Applicants state that the Examiner confirmed in a telephone interview on February 23, 2008 that there was a typographical error in the Office action. Specifically, the Examiner confirmed that claim 43 was in independent form, and thus that claims 43-47 were also in condition for allowance, thus, only claims 35, 50 and 54 were objected to for depending on a rejected base claim. Applicants state Clams 35, 50 and 54 are amended herein to be in independent form, placing claims 35, 50 and 54 in condition for allowance.

Applicants state that new claims 57-60 are added herein. These claims are added to subject matter previously included in claim 1, 25, 50 and 54. The addition of these new claims was previously discussed with the Examiner. Claims 58-60 but are limited to oligonucleotides "consisting of" the exact nucleotide sequences specified in allowed claim 1 is stated by Applicant. These claims were discussed with the Examiner on February 23, 2008. Applicants state that the Examiner requested that these claims be presented at the end of the claim set thus, new claims 58-60 should also be in condition for allowance.

Examiner's Response to Applicant's arguments:

Contrary to applicant's statement, the Examiner did not agree to any claims being condition for allowance. Examiner merely answered questions about specific claims that were objected or rejected but no specific discussion about allowable claims because a Primary Examiner was not present. Moreover, the statement "Claims 58-60 but are limited to oligonucleotides "consisting of" the exact nucleotide sequences specified in allowed claim 1" is is unclear.

New Grounds of Rejections

Claim Rejections - 35 USC § 112

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-5, 10, 12-13, 16, 18, 50, and 57-59 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is directed to the Guidelines for the Examination of Patent Applications under the 35 U.S.C. 112, first paragraph "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

In the instant case, the claims are drawn to a method of treating inflammatory lung disease in a subject, comprising administering a therapeutically effective amount of a suppressive oligodeoxynucleotide to a subject having inflammatory lung disease, wherein the suppressive oligodeoxynucleotide comprises the nucleic acid sequence set forth as one of SEQ ID NO: 1, or a combination of two or more thereof, thereby treating the inflammatory lung disease in the subject (claim 1); a method of treating or inhibiting acute respiratory distress syndrome in a subject, comprising administering locally a therapeutically effective amount of a suppressive oligodeoxynucleotide to a subject having or at risk of developing acute respiratory distress syndrome, wherein the suppressive oligodeoxynucleotide comprises from about 2 to about 4 guanosine-rich sequences, wherein the oligodeoxynucleotide comprises the nucleic acid sequence set forth as one of SEQ ID NO: 1, or a combination of two or more thereof (claim 50);

To fulfill the written description requirements set forth under 35 USC § 112, first paragraph, the specification must describe at least a substantial number of the members of the claimed genus, or alternatively describe a representative member of the claimed genus, which shares a particularly defining feature common to at least a substantial number of the members of the claimed genus, which would enable the skilled artisan to immediately recognize and distinguish its members from others, so as to reasonably convey to the skilled artisan that Applicant has possession the claimed invention. To adequately describe the genus of suppressive oligodeoxynucleotides aforementioned above, or a combination of two or more thereof, applicant must adequately which specific ODNs, if any, have efficacy to treat any type of inflammatory lung disease, reduce the production of a cytokine or chemokine, or treat or inhibit acute respiratory distress syndrome.

The specification discloses in Example 1 (see pp. 32-33), general methods and suppressive ODN H154 (SEQ ID NO: 1). The RAW 264.7 cells were incubated with 1μM ODN. The culture supernatant was analyzed for TNFα, MIP-2, IL-6, and KC content by ELISA. The mice were anesthetized with inhaled isoflurane. CpG, Neutral, and Suppressive ODN were administered intratracheally using a needle. Animals were sacrificed and the BAL fluid and cell culture supernatants' cytokine levels were measured. RT-PCR was conducted on the 264.7 cells incubated with 1μM ODN.

The specification discloses Example 2 (see pp. 34-35), suppressive ODN inhibit cytokine and chemokine production by RAW 246.7 cells. The RAW 264.7 murine macrophage cells were incubated with CpG ODN, alone or combined with suppressive ODN or neutral ODN (control). The specification indicates that Figure 2 show that suppressive ODN significantly reduces the production of TNFα and MIP-2 induced by CpG ODN.

The specification discloses Example 3 (see pp. 35-36); suppressive ODN block CpG-induced inflammation of the mouse lung. The RAW 264.7 cells murine macrophage cells were incubated with E.coli DNA, alone or combined with suppressive ODN or neutral ODN (control). The specification indicates that Figures 3 and 4 shows that suppressive ODN significantly reduces the production of TNFα and MIP-2 induced by CpG ODN.

The specification does not give a final analysis of Example 1. The specification does not indicate that the RAW murine macrophage 264.7 cells mimics human lung disorders in Example 1. The specification does not give a clear and concise reason as to the use of the mice cells in addition to the RAW 264.7 cells. The specification does not state which ODN is being incubated and which ODNs are being administered to the mice. The data from Examples 2 and 3 teach treatment as defined in the specification, "therapeutic intervention that ameliorates a sign or symptom of a disease or pathological condition after it has begun to develop" (p. 18 line 1). These disclosures do not provide adequate description of the claimed genus suppressive oligodeoxynucleotides aforementioned above, or a combination of two or more thereof.

Applicant has not demonstrated that suppressive oligodeoxynucleotides aforementioned above, or a combination of two or more thereof possess treating inflammatory lung disease, reducing the production of a cytokine or chemokine, or treating or inhibiting acute respiratory distress syndrome. The limited number of suppressive oligodeoxynucleotides aforementioned above or a combination of two or more thereof disclosed is not deemed to be representative of the genus encompassed by the instant claims. The specification, does not disclose distinguishing and identifying features of a representative number of members of the genus of suppressive oligodeoxynucleotides aforementioned above, or a combination of two or more thereof, to which the claims are drawn, such as a correlation between the structure of the suppressive oligodeoxynucleotides aforementioned above, or a combination of two or more thereof and its recited function treating inflammatory lung disease, reducing the production of a cytokine or chemokine, or treating or inhibiting acute respiratory distress syndrome so that the skilled artisan could immediately envision, or recognize at least a substantial number of members of the claimed genus of suppressive oligodeoxynucleotides aforementioned above, or a combination of two or more thereof.

Based on the teachings in the specification and the demonstration by Applicant in data presented in the specification of the in vivo data, suppressive ODN co-administered with CPG reduced the production of IL-6, MIP-2m, and KC significantly, and in vitro data of RAW 264.7 cells murine macrophage cells incubated with a suppressive ODN significantly reduces the production of proinflammatory molecules, one skilled in the art would not expect the in vivo data or in vitro data aforementioned above to be consistent with treating an inflammatory lung disease comprising administering a suppressive oligodeoxynucleotide. Furthermore one skilled in the art would not except no *in vivo* data provided to be directed to the claimed invention.

Although the specification contemplates that the same results one would occur *in vitro* would function *in vivo* and vice versa, the specification does not provide any evidence that any of the claimed methods would function *in vivo*. The issue of correlation is related to the issue of the presence or absence of working examples. Correlation as used herein refers to the relationship between *in vitro* or *in vivo* animal model assays and disclosed or a claimed method of use. An *in vitro* or *in vivo* animal model example in the specification, in effect, constitutes a working example, if that example correlates with a disclosed or claimed method invention. Also *in vitro* data does not necessarily correlate with *in vivo* efficacy. If there is no correlation, then the examples do not as constitute working examples.

Moreover, Examples 1, 2, and 3 do not teach inhibiting of acute respiratory disease syndrome. However the rejected claims are directed to a method of treating inflammatory lung disease in a subject, comprising administering a therapeutically effective amount of a suppressive oligodeoxynucleotide to a subject having inflammatory lung disease, wherein the suppressive oligodeoxynucleotide comprises the nucleic acid sequence as set forth supra, or a combination of two or more thereof, aforementioned above excluding solely SEQ ID NO:1 (claims 1-5, 10, 12-13, 16, 18, and 57-58); a method of treating or inhibiting acute respiratory distress syndrome in a subject, comprising administering locally a therapeutically effective amount of a suppressive oligodeoxynucleotide to a subject having or at risk of developing acute respiratory distress syndrome, wherein the suppressive oligodeoxynucleotide comprises from about 2 to about 4 guanosine-rich sequences, wherein the oligodeoxynucleotide comprises the nucleic acid sequence as set forth supra, or a combination of two or more thereof, aforementioned above excluding solely SEQ ID NO:1 (claims 50 and 59) and do not meet the written description requirements.

MPEP § 2163.02 states, "[a]n objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed' ". The courts have decided:

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed*.

See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.,* 18 USPQ2d 1016.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description" Requirement (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). Moreover, because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant were in possession of the claimed invention at the time the application was filed. The *Guidelines* further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species *cannot* be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus.

Therefore, absent a detailed and particular description of a representative number, or at least a substantial number of the members of the genus aforementioned above, the skilled artisan could not immediately recognize or distinguish members of the claimed genus of suppressive oligodeoxynucleotides aforementioned above, or a combination of two or more thereof with the recited activities. Therefore, because the art is unpredictable, in accordance with the *Guidelines*, the description of suppressive oligodeoxynucleotides aforementioned above is not deemed representative of the genus of suppressive oligodeoxynucleotides aforementioned above, or a combination of two or more thereof to which the claims refer and therefore the claimed invention is not properly disclosed eventhough SEQ ID NO:1 meet the written description provision of 35 USC 112, first paragraph.

Enablement

6. Claims 1-5, 10, 12, 13, 16, 18, 43-45, 50, and 57-59 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contain subject matter, which was not described in the specification in such a way as to enable one

skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Furthermore, the specification does not reasonably enable any method of treating inflammatory lung disease in a subject, comprising administering a therapeutically effective amount of a suppressive oligodeoxynucleotide (ODN) to a subject having inflammatory lung disease, wherein the suppressive oligodeoxynucleotide comprises the nucleic acid sequence set forth as one of SEQ ID NO: 1, or a combination of two or more thereof, thereby treating the inflammatory lung disease in the subject (claim 1); a method of treating acute respiratory distress in a subject, comprising administering to the subject by inhalation a therapeutically effective amount of an oligodeoxynucleotide comprising the nucleic acid sequence set forth as SEQ ID NO: 1, thereby treating the acute respiratory distress in the subject (claim 43); a method of treating or inhibiting acute respiratory distress syndrome in a subject, comprising administering locally a therapeutically effective amount of a suppressive oligodeoxynucleotide to a subject having or at risk of developing acute respiratory distress syndrome, wherein the suppressive oligodeoxynucleotide comprises from about 2 to about 4 guanosine-rich sequences, wherein the oligodeoxynucleotide comprises the nucleic acid sequence set forth as one of SEQ ID NO: 1, or a combination of two or more thereof (claim 50). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claimed invention.

Enablement is considered in view of the *Wands* factors (MPEP 2164.01(a)).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to:

(A) The breadth of the claims;

(B) The nature of the invention;

(C) The state of the prior art;

(D) The level of one of ordinary skill;

(E) The level of predictability in the art;

(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Nature of the invention: The instant claims are drawn to any method of treating inflammatory lung disease in a subject, comprising administering a therapeutically effective amount of a suppressive oligodeoxynucleotide to a subject having inflammatory lung disease, wherein the suppressive oligodeoxynucleotide comprises the nucleic acid sequence set forth as one of SEQ ID NO: 1, or a combination of two or more thereof, thereby treating the inflammatory lung disease in the subject (claim 1); a method of treating or inhibiting acute respiratory distress syndrome in a subject, comprising administering locally a therapeutically effective amount of a suppressive oligodeoxynucleotide to a subject having or at risk of developing acute respiratory distress syndrome, wherein the suppressive oligodeoxynucleotide comprises from about 2 to about 4 guanosine-rich sequences, wherein the oligodeoxynucleotide comprises the nucleic acid sequence set forth as one of SEQ ID NO: 1, or a combination of two or more thereof (claim 50).

Breadth of the claims: The breadth of the claims is very broad and the quantity of experimentation required is undue. The product being used to administer to a subject (human or otherwise) stated in the instant claims, a suppressive oligodeoxynucleotides aforementioned above, or a combination of two or more thereof to treat inflammatory lung disease which encompasses different types of inflammatory lung diseases comprising acute respiratory distress syndrome, pneumonia, respiratory distress prematurity, chronic bronchitis, chronic obstructive pulmonary disease, cystic fibrosis, pulmonary fibrosis, or pulmonary sarcoidosis is overly broad. Furthermore, the product comprising a suppressive oligodeoxynucleotide aforementioned above or a combination of two or more thereof to treat inflammatory lung disease or a method of treating or inhibiting acute respiratory distress syndrome in a subject is also overly broad. Therefore it is hard for one skilled in the art to determine if any suppressive oligodeoxynucleotide can be used in treating inflammatory lung disease and furthermore treating or inhibiting acute respiratory distress syndrome in a subject and therefore be deemed a suppressive oligodeoxynucleotide. Since the specification fails to provide particular guidance for the treatment of inflammatory lung disease and furthermore treating or inhibiting acute respiratory distress syndrome in a subject, it would require undue experimentation to practice the invention over the broad scope as presently claimed.

Guidance of the specification/The existence of working examples:

The specification discloses in Example 1 (see pp. 32-33), general methods and suppressive ODN H154 (SEQ ID NO:1). The RAW 264.7 cells were incubated with 1μM ODN. The culture supernatant was analyzed for TNFα, MIP-2, IL-6, and KC content by ELISA. The mice were anesthetized with inhaled isoflurane. CpG, Neutral, and Suppressive ODN were administered intratracheally using a needle. Animals were sacrificed and the BAL fluid and cell culture supernatants' cytokine levels were measured. RT-PCR was conducted on the 264.7 cells incubated with 1μM ODN.

The specification discloses Example 2 (see pp. 34-35), suppressive ODN inhibit cytokine and chemokine production by RAW 246.7 cells. The RAW 264.7 murine macrophage cells were incubated with CpG ODN, alone or combined with suppressive ODN or neutral ODN (control). The specification indicates that Figure 2 show that suppressive ODN significantly reduces the production of TNFα and MIP-2 induced by CpG ODN.

The specification discloses Example 3 (see pp. 35-36); suppressive ODN block CpG-induced inflammation of the mouse lung. The RAW 264.7 cells murine macrophage cells were incubated with E.coli DNA, alone or combined with suppressive ODN or neutral ODN (control). The specification indicates that Figures 3 and 4 shows that suppressive ODN significantly reduces the production of TNFα and MIP-2 induced by CpG ODN. The data from Examples 2 and 3 teach treatment as defined in the specification, "therapeutic intervention that ameliorates a sign or symptom of a disease or pathological condition after it has begun to develop" (p. 18 line 1).

The specification is only limited to a method of reducing the production of a cytokine and chemokine in RAW 246.7 cells and in a mouse model. The specification does not give a final analysis of Example 1. The specification does not indicate that the RAW murine macrophage 264.7 cells mimics human lung disorders in Example 1. The specification does not give a clear and concise reason as to the use of the mice cells in addition to the RAW 264.7 cells. The working examples do not disclose any empirical data or results indicative of a method of treating any specific inflammatory lung disease and furthermore a method of treating or inhibiting of acute respiratory disease syndrome. Therefore the data fails to show the claimed invention aforementioned above. The specification is devoid of data that indicates that the broadly claimed ISS nucleic acids possess immunostimulatory activity as claimed.

Furthermore, the specification states that "CpG motifs have been shown to cause inflammation of the lower respiratory tract" and "CpG ODN can be used as a surrogate for bacterial DNA in studying lung inflammation, and CpG-induced lung inflammation is a useful model for studying other more typical causes of inflammatory lung disease" (see Example 2). Therefore the specification merely contemplates the claimed invention. Therefore, one skilled in the art would not accept on its face the examples given in the specification as being correlative or representative of a successful model. The specification is devoid of any teaching that the claimed invention treats any specific inflammatory lung disease and furthermore a method of treating or inhibiting of acute respiratory disease syndrome.

Based on the teachings in the specification and the demonstration by Applicant in data presented in the specification of the *in vivo* data, suppressive ODN co-administered with CPG reduced the production of IL-6, MIP-2m, and KC significantly, and *in vitro* data of RAW 264.7 cells murine macrophage cells incubated with a suppressive ODN significantly reduces the production of proinflammatory molecules, one skilled in the art would not expect the in vivo data or in vitro data aforementioned above to be consistent with treating an inflammatory lung disease comprising administering a suppressive oligodeoxynucleotide. Furthermore one skilled in the art would not except the no *in vivo* data provided as directed to the claimed invention and that *in vitro* data does not necessarily correlate with *in vivo* efficacy.

Although the specification contemplates that the same results one would occur *in vitro* would function *in vivo* and vice versa, the specification does not provide any evidence that any of the claimed methods would function *in vivo*. The issue of correlation is related to the issue of the presence or absence of working examples. Correlation as used herein refers to the relationship between *in vitro* or *in vivo* animal model assays and disclosed or a claimed method of use. An *in vitro* or *in vivo* animal model example in the specification, in effect, constitutes a working example, if that example correlates with a disclosed or claimed method invention. Also *in vitro* data does not necessarily correlate with *in vivo* efficacy. If there is no correlation, then the examples do not as constitute working examples.

State of the art: The state of the prior art is unpredictable with regard to inflammatory lung disease treatments using suppressive oligodeoxynucleotides and furthermore treating or inhibiting acute respiratory distress syndrome. The art indicates most CpG containing oligonucleotides are currently being investigated for exerting their immunotherapeutic effects in various organisms. The art state that using an animal model that mimics key aspects of human inflammatory lung disease has been limited. “The lack of animal model that unequivocally mimics key aspects of human ALI/ARDS has been limiting in mechanistic studies and in providing meaningful and rapid extrapolations to the clinical syndrome” (see Matthay et al 2003 *American Journal Respiratory Critical Care Medicine* Vol 167. p. 7). Van der Vliet et al state that “two general research approaches have been taken: the use of pharmacological inhibitors of NOS isoenzymes, and the targeted deletion of individual NOS enzymes in mice. Both approaches suffer from the short-coming that animal models of respiratory tract diseases generally do no faithfully reflect human disease” (see Van der Vliet et al 2000 Respiratory Res Vol 1 No. 2. p. 68). The art for treating and preventing inflammatory lung disease are using current treatments such as anti-inflammatory medications. Although inflammatory lung disease can be treated there is no treatment for recurrence or prevention of the full development of the disease. The standard therapy for treating inflammatory lung disease is corticosteroids. However they also have limitations in their treatment and cannot inhibit inflammatory lung disease (see Broide et al 1998 Immunostimulatory DNA Sequences Inhibit IL-5, Eosinophilic Inflammation, and Airway Hyperresponsiveness in Mice The Journal of Immunology p. 7054 and Bernard GR 2005 Acute respiratory distress syndrome: a historical perspective. *American Journal Respiratory Critical Care Med.* 2005 Oct 1;172(7):798-806).

Therefore, the state of the art shows that there are limitations on anti-inflammatory medications for treating and inhibiting/preventing inflammatory lung disease in a subject; and in addition to the current treatment discussed above, the state of the art is unpredictable with regard to the use of CpG-ODN in treating and inhibiting/preventing inflammatory lung disease in a subject (human or otherwise) at risk for an inflammatory lung disease. Lastly, there is no information on administering suppressive oligodeoxynucleotide (ODN) to a subject (human or otherwise) for a method of treating inflammatory lung disease nor a method of treating or inhibiting acute respiratory distress syndrome. For the reasons set forth supra, the state of the art on the current medications have limitations and the state of the art on suppressive oligodeoxynucleotides is unpredictable with regard to the claimed invention.

The state of the art several years after Applicants' effective filing date teaches that methods claimed by Applicants are still not enabled.

In general, the examiner should not use post-filing date references to demonstrate that the patent is non-enabling. Exceptions to this rule could occur if a later-dated reference provides evidence of what one skilled in the art would have known on or before the effective filing date of the patent application. *In re Hogan*, 559 F.2d 595, 605, 194 USPQ 527, 537 (CCPA 1977). If individuals of skill in the art state that a particular invention is not possible years after the filing date, which would be evidence that the disclosed invention was not possible at the time of filing and should be considered. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513-14 (Fed. Cir. 1993) An article published 5 years after the filing date of the application adequately supported the examiner's position that the physiological activity of certain viruses was sufficiently unpredictable so that a person skilled in the art would not have believed that the success with one virus and one animal could be extrapolated successfully to all viruses with all living organisms. Claims not directed to the specific virus and the specific animal were held nonenabled (See MPEP 2164.05(a)).

In conclusion, the claimed invention is not enabled for any method of treating inflammatory lung disease in a subject or a method of treating or inhibiting acute respiratory distress syndrome in a subject comprising administering a therapeutically effective amount of a suppressive oligodeoxynucleotide aforementioned above. The product being used to administer to a subject (human or otherwise) stated in the instant claims, a suppressive oligodeoxynucleotides aforementioned above, or a combination of two or more thereof to treat inflammatory lung disease which encompasses different types of inflammatory lung diseases comprising acute respiratory distress syndrome, pneumonia, respiratory distress prematuriy, chronic bronchitis, chronic obstructive pulmonary disease, cystic fibrosis, pulmonary fibrosis, or pulmonary sarcoidosis is overly broad. Furthermore, the product comprising a suppressive oligodeoxynucleotide aforementioned above or a combination of two or more thereof to treat inflammatory lung disease or a method of treating or inhibiting acute respiratory distress syndrome in a subject is also overly broad. The specification is devoid of any teaching that the claimed invention treats any specific inflammatory lung disease and furthermore a method of treating or inhibiting of acute respiratory disease syndrome. The state of the art on the current medications have limitations and the state of the art on suppressive oligodeoxynucleotides is unpredictable with regard to the claimed invention. In view of the lack of support in the art and specification for the claimed invention; therefore the claims are not enabled. As a result, for the reasons discussed above, it would require undue experimentation for one skilled in the art to use the claimed invention.

Claim Rejections - 35 USC § 112

> The following is a quotation of the second paragraph of 35 U.S.C. 112:
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

7. Claims 12, 16, 35, and 50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claims 12, 16, 35, and 50 recites the phrase “from about 2 to about 4”. However, neither the claim nor the specification clearly defines nor sets forth the meaning or means to assess "from about 2 to about 4". There is no art define meaning in regards to the method "from about 2 to about 4". Therefore, the skilled artisan would not be readily apprised of the metes and bounds of "from about 2 to about 4" nor how to assess such. It is unclear how to interpret what is considered "from about 2 to about 4" and inasmuch as it is not a recognized term and not defined in the specification.

Conclusion

8. No claims allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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